Quantitative Susceptibility Mapping: A Potential Biomaker for Characterizing Cerebral Cavernous Malformation

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Introduction: Cerebral cavernous malformation (CCM) is a common hemorrhagic vascular anomaly of the human brain, characterized by repetitive lesional hemorrhages. Susceptibility weighted imaging (SWI), a qualitative MRI technique, has a high sensitivity for detecting CCM lesions (1). However, SWI has only been used to assess lesion counts and volume, and does not provide a means to evaluate changes in iron distribution within individual lesions. A new technique, quantitative susceptibility mapping (QSM), allows quantitative evaluations of intra-lesional susceptibility changes related to leakage of iron-containing blood products. Another unique attribute of QSM is the ability to distinguish cerebral hemorrhage from calcifications (a common finding in this population), which SWI lacks (2). In the present study, we performed QSM in patients with CCM to characterize lesion burden in terms of lesion count, size and susceptibility values. The long term goal is to evaluate the potential of QSM as a new quantitative imaging marker for monitoring CCM lesion progression and/or responses to treatments.

Methods: A total of 9 CCM patients were recruited for the study under the supervision of our institutional revision board. All imaging was performed on a Siemens 3T scanner (MAGNETOM Verio, Siemens Healthcare, Erlangen, Germany) with a 12 channel phased array head coil. A single three dimensional, multi-echo, T2*-weighted, spoiled gradient echo sequence was used for data collection for both SWI and QSM reconstruction. The imaging parameters were as follows: axial imaging plane with full brain coverage; 8 echo times with uniform spacing; TE [min, max] = [3.6, 45] ms; TR = 55 ms; flip angle = 15°; bandwidth = 240 Hz/Pixel; field of view = 240 mm, acquisition matrix = 256 x 256; slice thickness = 1.5 mm; number of slab encodings = 80. Data acquisition is accelerated by a factor of 2 with iPAT. The imaging time is 7 minutes and 40 seconds.

The SWI and QSM images were reconstructed offline using customized software. Data from the longest echo time (TE = 45ms) was used for SWI reconstruction. QSM images were reconstructed using a morphology-enabled dipole inversion (MEDI) algorithm (3). Regions of interest (ROIs) within the lesions were defined on SWI images using a semi-automatic algorithm utilizing thresholding and region-grow method. Susceptibility values were measured using the ROI masks defined by SWI.

Results: Magnetic susceptibility from blood byproducts such as deoxyhemoglobin and hemosiderin present in the CCM lesions resulted in a dark signal on SWI. In contrast, these lesions appeared bright on QSM. Figure 1 illustrates one solitary sporadic CCM case. The CCM lesion can be identified on both QSM and SWI. However, calcification in choroid plexus (arrow) appeared dark on QSM due to its diamagnetic properties, and can be easily distinguished from the bright CCM lesion. Such distinction was not possible with SWI, where both CCM lesion and calcifications appeared hypointensive.

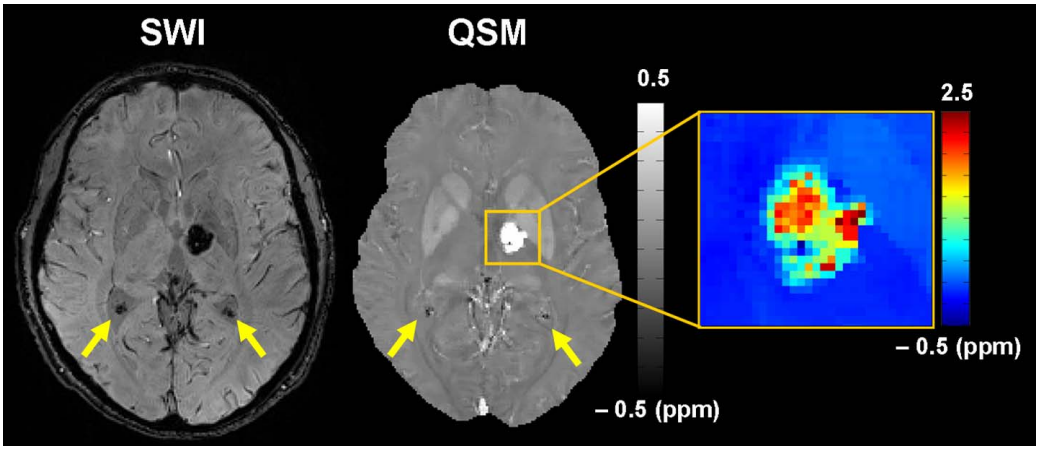

Figure 1. Examples of QSM and SWI from a CCM patient (age 45, male). The CCM lesion and calcifications were clear distinguishable on QSM. The susceptibility distribution within the CCM lesion is displayed on the right.

There were 6 subjects with solitary and 3 with multi-focal lesions in our patient population. The lesion volume varied from 5 – 7280 mm^3. The mean susceptibility varied from 0.36 – 0.72 ppm across all lesions. The averaged mean susceptibility is 0.56 ± 0.15 ppm for the CCM lesions and –0.38 ± 0.7 ppm for the calcifications in the choroid plexus. Larger lesions were observed to have higher susceptibility values suggesting higher iron content in the lesion.

Conclusions: Our preliminary results have demonstrated the QSM's unambiguous ability to separate iron-rich CCM lesions from calcification, and to provide quantitative evaluation of the lesion. QSM offers a complementary strategy aiming to quantify local iron deposit within individual lesions, which is the ultimate manifestation of clinical CCM sequelae. In addition, QSM was previously shown to have reduced variation in terms of lesion size over a wide spectrum of echo times, when compared to SWI (4). Gradient echo MRI contains rich ties magnetic property. While SWI is useful to improve susceptibility lesion conspicuity, a new field-to-susceptibility inverse solution based QSM may serve as a novel imaging biomarkers to provide quantitative monitoring of iron content in individual lesions of CCM disease progression.

Reference: 1) de Champfleur et al. Neurosurgery, 2011. 2) Schweser et. al. Med Phys, 2010. 3) Liu et al. Magn Reson Med, 2011. 4) Liu et al. Radiology, 2011.